Amendments to the Claims:

1-22. (Canceled)

23. (Withdrawn) A method of ordering pairs of sequence tags, the method comprising the steps of:

a) providing a population of pairs of sequence tags of restriction fragments, produced by digesting a fragment of genomic DNA with a plurality of combinations of restriction endonucleases;

b) removing duplicate pairs of sequence tags from the population;

c) selecting a pair of sequence tags from the population;

d) comparing each sequence tag of the selected pair with each sequence tag of a first pair and a last pair of a candidate ordering;

e) adding the selected pair to an end of the candidate ordering whenever a sequence tag of the selected pair matches the sequence tag of the first pair or the last pair of the candidate ordering, to form a new candidate ordering; and

f) repeating steps c) through e) until all pairs of the population have been selected.

24. (Withdrawn) The method of claim 23, wherein each population of pairs of sequence tags consists of n pluralities of pairs of sequence tags, each plurality being formed by digesting said fragment of genomic DNA in n separate reactions, each with a different n-1 combination of restriction endonucleases, wherein each pair of sequence tags is formed by ligating a portion of each end of each restriction fragment together.

25. (Withdrawn) The method of claim 24, wherein said population of pairs of sequence tags consists of samples of pairs of sequence tags from each of said n pluralities.

26. (Withdrawn) The method of claim 25, wherein each of said samples has the same size.

27. (Withdrawn) The method of claim 26, wherein n =3 and each said restriction endonuclease has a six-basepair recognition site.

28. (Currently amended) ~~An oligonucleotide composition~~ A plurality of oligonucleotides derived from restriction fragments of a polynucleotide, ~~genomic DNA, said composition comprising: a plurality of oligonucleotides, each containing a ligated pair of sequence tags, wherein~~

each said ~~ligated pair of sequence tags is from nine to eighteen basepairs in length and consists of opposite~~ oligonucleotide containing first and second end segments from opposite ends of ~~a single said~~ one such restriction fragment ~~of said genomic DNA~~, wherein

said first end segment consists of a first end sequence, having 5 to 12 basepairs, immediately adjacent to a cleaved restriction site,

said second end segment consists of a second end sequence, having 5 to 12 basepairs, immediately adjacent to a cleaved restriction site,

and said first and second end sequences are ligated together;

wherein each end sequence contains the same number of basepairs;

and wherein each end sequence is unique.

29. (Previously presented) The oligonucleotide composition of claim 28, wherein each said restriction fragment has ends produced by digestion with different restriction endonucleases.

30. (Previously presented) The oligonucleotide composition of claim 29, wherein each said restriction fragment has ends produced by digestion of two different restriction endonucleases selected from a group consisting of three different restriction endonucleases.

31. (Previously presented) The oligonucleotide composition of claim 30, wherein each of said three different restriction endonucleases has a six-basepair recognition site.

32. (Currently amended) The oligonucleotide composition of claim 28, wherein said plurality ~~of~~ includes a number of oligonucleotides ~~is a sample having a size~~ sufficient to contain with a probability of ninety-nine percent at least one copy of said first and second ~~pairs of~~ sequence tags from each of said restriction fragments of said polynucleotide ~~genomic DNA~~.

33. (Cancelled)

REMARKS

Reconsideration of the rejections set forth in the Office action mailed March 17, 2005 is respectfully requested. Claims 23-32 are pending, claim 33 having been cancelled with the amendment. Claims 28-32 are under examination, and claims 23-27 are currently withdrawn from consideration.

I. Amendments

Claim 28 is amended for clarity and to more particularly point out the features of the claimed composition. The claim also incorporates the subject matter of cancelled claim 33.

Support for the claim phrase "restriction fragments of a polynucleotide" is found, for example, at page 5, line 10 of the specification, and at page 7, lines 18-20, which refers several times to the target "polynucleotide".

Support for each end sequence having "5 to 12 basepairs" and being "immediately adjacent to a cleaved restriction site" is found, for example, at page 5, line 12, and at page 7, lines 18-35, which describes end segments consisting of unique sequences (i.e., tags) adjacent to restriction sites. See in particular lines 23-28 regarding length of the unique sequences ("the number of nucleotides determined could be as low as five or six ... 9-12 nucleotides are preferably determined to ensure that the end sequences are unique"), and lines 25-26 and 29-31 regarding the unique sequence being adjacent to a cleaved recognition site ("at least 8 nucleotides are determined in the regions adjacent to restriction sites" and "type IIs enzymes having a (16/14) reach effectively provide *9 bases of unique sequence* (since blunting reduces the number of bases to 14 and *5 bases are part of the recognition sites*..." (emphasis added). This can also be understood from the description of Figure 2 in the subsequent paragraph, at page 8, lines 1-10.

The subject matter of claim 33, regarding the end sequences being equal in length, has been incorporated into claim 28.

The paragraph at page 7, lines 18-35 also provides support for the added clause in claim 28, "wherein each said end sequence is unique". See, for example, lines 18-20 ("a type IIs restriction endonuclease for generating pairs of segments has as great a reach as possible to maximize the probability that the nucleotide sequences of the segments are unique"), 24-25

("...the number of nucleotides determined could be as low as five or six, and still have a significant probability that each end sequence would be unique"), and 27-28 ("for polynucleotides less than or equal to 10 megabases, 9-12 nucleotides are preferably determined to ensure that the end sequences are unique"). This feature ensures that each end sequence is effective to uniquely identify the restriction fragment from which it was derived. See e.g. page 9, lines 31-33: "In a polynucleotide having a random sequence of nucleotides, a 9-mer appears on average about once every 262,000 bases. Thus, 9-mer sequences are quite suitable for uniquely labeling restriction fragments...".

Claim 32 is also amended for clarity, and for consistency with amended claim 28.

No new matter is added by any of the amendments.

II. Claim Objections

The suggested amendment to claim 28 and the second suggested amendment to claim 32 have been made. However, the first suggested amendment to claim 32 is rendered moot by the other amendments to this claim.

III. Rejections under 35 U.S.C. §102(b)

Independent claim 28 and its dependent claims were rejected under 35 U.S.C. §102(b) as being anticipated by New England Biolabs 96/97 Catalog, page 115. This rejection is respectfully traversed for the following reasons.

A. The Claims

Independent claim 28 is directed to a plurality of oligonucleotides derived from restriction fragments of a polynucleotide, each said oligonucleotide containing first and second end segments from opposite ends of one such restriction fragment, wherein

said first end segment consists of a first end sequence, having 5 to 12 basepairs, immediately adjacent to a cleaved restriction site,

said second end segment consists of a second end sequence, having 5 to 12 basepairs, immediately adjacent to a cleaved restriction site,

and said first and second end sequences are ligated together;

wherein each end sequence contains the same number of basepairs; and wherein each end

sequence is unique.

The last recited feature provides that each end sequence is effective to uniquely identify the restriction fragment from which it was derived (see e.g. page 9, lines 32-33).

B. The Prior Art

The cited catalog page shows a series of adaptors for interconversion of restriction sites on polynucleotides. Generally, the adaptors have restriction sites for different enzymes at their ends and may include internal spacer groups.

The only adaptors in which the spacer group is long enough to meet the length requirement for "first and second end sequences" (which would be 10 to 24 basepairs in combined length, each being 5 to 12 basepairs) are those designated "#1184" and "#1187" (each duplexed with "#1188"). These adaptors are reproduced below:

```
                GCCGGTTTTTCCGG                      #1188
          GATCCGGCCAAAAAGGCCTGCA                    #1184
protruding end      spacer      protruding end
from BamHI                      from PstI
cleavage                        cleavage

                GCCGGTTTTTCCGG                      #1188
          AATTCGGCCAAAAAGGCCTGCA                    #1187
protruding end      spacer      protruding end
from EcoRI                      from PstI
cleavage                        cleavage
```

It can be seen that the spacer groups in the two adaptors shown above are identical.

Independent claim 28 recites that (i) "each end sequence contains the same number of basepairs" and that (ii) "each end sequence is unique".

In accordance with (i), which requires that the ligated "end sequences" are equal in length, the "end sequences" in #1184 would be GGCCAA and AAAGGC (each in duplex form). The "end sequences" in #1187 would also be GGCCAA and AAAGGC (each in duplex form).

Accordingly, the "plurality of oligonucleotides" represented by these two adaptors does not meet the requirement of (ii); i.e. that "each end sequence is unique", since the "end sequences" in #1184 are identical to the "end sequences" in #1187.

Applicants submit that the reference does not disclose all of the elements set out above in claim 28 and its dependent claims 29-33. In view of this, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §102(b).

IV. Rejections under 35 U.S.C. §102(e)

Independent claim 28 and its dependent claims were rejected under 35 U.S.C. §102(e) as being anticipated by Sapolsky *et al.*, U.S. Patent No. 5,710,000. This rejection is respectfully traversed for the following reasons.

A. The Claims

The subject matter of independent claim 28 is described above.

B. The Prior Art

The Examiner has interpreted the disclosure of Sapolsky *et al.*, in which different type IIs recognition sites, each recognition site being 9-18 basepairs in length, are located on opposite ends of restriction fragments, as teaching the limitations of independent claim 28.

The Examiner asserts that the claims as previously presented did not require that the pair of ligated sequence tags (now termed end sequences) be directly connected to each other (page 7 of Office Action).

The independent claim as amended now clearly recites that "said first and second end sequences are ligated together".

Applicants submit that the reference does not disclose all of the elements set out above in claim 28 and its dependent claims 29-33. In view of this, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §102(e).

V. Rejections under 35 U.S.C. §102(b)

Independent claim 28 and its dependent claims were rejected under 35 U.S.C. §102(b) as being anticipated by Morgante *et al.*, PCT Pubn. No. WO 96/17082. The rejections are respectfully traversed in light of the following remarks.

A. The Claims

The subject matter of independent claim 28 is described above.

B. The Cited Art

Morgante *et al.* teach the ligation of synthetic oligonucleotide adaptors to the ends of DNA restriction fragments. As described at page 51, lines 6-10 of the PCT specification, the adaptors are at least 10 nucleotides long, preferably at least 12 nucleotides long. As described at page 51, lines 6-10 of the PCT specification, the restriction fragments "receive adaptors at both ends". Therefore, the resulting adaptor-fragment-adaptor constructs would have to be greater than 20 nucleotides in length, and would typically be much longer, depending on the length of the fragment. Moreover, the adaptors are not ligated to each other, but to both ends of a DNA fragment.

The Examiner asserts that the claims as previously presented did not require that the pair of ligated sequence tags (now termed end sequences) be directly connected to each other (page 10 of Office Action).

The independent claim as amended now clearly recites that "said first and second end sequences are ligated together".

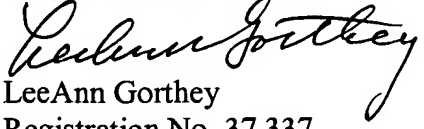
Applicants submit that the reference does not disclose all of the elements set out above in claim 28 and present in dependent claims 29-33. In view of this, the applicant respectfully requests the Examiner to withdraw this rejection.

VI. Conclusion

In view of the foregoing, the applicant submits that the claims under examination are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4403.

Respectfully submitted,



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